REMARKS

In a non-final Office Action dated January 7, 2008, the Examiner rejected selected claims under 35 U.S.C. §§ 112 and 102(e). The Examiner indicated that Claims 1-29 and 51 are pending, but that Claims 3-6, 8-9, 11-12, 14-15, 21-22, 24 and 26 are withdrawn from consideration, and indicated that Claims 17-18, 28 and 51 are allowed. Applicants respond to each of the Examiner's rejections below. In view of the amendments above and the remarks below, Applicants respectfully request reconsideration of the merits of this application. Applicants respectfully request a timely Notice of Allowance.

Rejection Under 35 U.S.C. § 112

The Examiner rejected Claims 1-2, 7, 10, 13, 16, 19-20, 23, 25, 27 and 29 under 35 U.S.C. § 112, second paragraph, for being indefinite. The Examiner alleged that the claims do not link the recited amino acid positions for SCN5A to a sequence/structure for SCN5A. Applicants amend Claim 1 to recite that the polynucleotide encodes SEQ ID NO:8 or a complement of SEQ ID NO:8. In view of this amendment, Applicants respectfully request reconsideration of this rejection as applied to the claims.

Rejection Under 35 U.S.C. § 102(e)

The Examiner maintained the rejection of Claims 1-2, 7, 10, 13, 16-20, 23, 25 and 27-29 are rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,342,357 to Splawski & Keating. The Examiner alleged that Splawski & Keating anticipates the claims by disclosing a nucleic acid encoding a SCN5A polypeptide having an alteration at amino acid position 552 (arginine instead of glycine) that is 99.5% identical to SEQ ID NO:8. Applicants amend Claims 1 and 20 to recite that the polynucleotide encodes SEQ ID NO:8 or a complement of SEQ ID NO:8.

Splawski & Keating cannot anticipate the amended claims because it does not disclose SEQ ID NO:8. Instead, Splawski & Keating discloses a polypeptide that differs from the encoded polypeptide at amino acid positions 552, 558, 618, 1027 and 1077.

As described in the application, the SCN5A sequences presented and claimed represent the most common in the human population. In contrast, the sequences disclosed in Splawski & Keating are not. Applicants examined over one-hundred SCN5A variants to identify the most

common sequences in the general population. Until the Applicants' discovery, diagnostic and screening methods used rare variants, such as the one disclosed in Splawski & Keating, which were less applicable to the general population. Such rare variants are of limited diagnostic value to a potential licensee, such as a drug company, because any data obtained using the rare variants would not necessarily apply to the general population.

Moreover, the application demonstrates the importance of selecting a proper background sequence when evaluating cardiac sodium channels, as rare SCN5A variants show unpredictable results/phenotypes. For example, FIGS. 3 and 5-6 of the application show that current, current density, effect of β1-subunit, and protein trafficking differed among the SCN5A variants. These results were not predictable based upon the variants previously disclosed including that of Splawski & Keating. Thus, new diagnostic and screening methods employing the claimed SCN5A sequence increase the ability to predict outcome in a greater percentage of the general population. Also, knowing the SCN5A background allows for tailored treatment strategies (*see*, paragraph [0045] of the application).

The application also discloses the importance of recognizing the common SCN5A sequences and that mutations harbored in SCN5A variants differentially affected the pathology of diseases such as LQT syndrome and other cardiac arrhythmias. Even single amino acid differences in the SCN5A polypeptide can have drastic effects. For example, the application shows that a M1766L mutation introduced into the disclosed SCN5A polypeptides affected protein trafficking only for some variants, but not all (Q1077del;M1766L vs. H558R;Q1077del;M1766L). The effect of the M1766 mutation on the various SCN5A polypeptides was not obvious.

With respect to Splawski & Keating, it cannot be said that the claimed nucleic acids and encoded polypeptides are anticipated or obvious, as one of ordinary skill in the art cannot readily predict the existence or effect of one mutation versus another in a nucleic acid or polypeptide in a SCN5A variant. In view of the amendments above and the remarks herein, Applicants respectfully request reconsideration of this rejection as applied to Claims 1-2, 7, 10, 13, 16-20, 23, 25 and 27-29.

Additional Remarks

In view of the amendments made to Claim 1, Applicants cancel Claims 2-16. Applicants also add new Claim 52, which recites that claimed polynucleotide comprises SEQ ID NO:7.

In view of the amendments made to Claim 20, Applicants cancel Claims 21-27 and amend Claim 28 to include the limitation in Claim 51. Accordingly, Applicants also cancel Claim 51.

Applicants also include a Supplemental Information Disclosure Statement (IDS) with this submission. The Supplemental IDS contains four documents cited in corresponding European Patent Application No. 03767086.6.

GenBank Accession No. AY038064 and WO 96/28537 were cited as affecting the novelty of the claims. GenBank Accession No. AY038064 discloses an amino acid that differs from SEQ ID NO:8 at amino acid position 552. WO 96/28537, related to Splawski & Keating, differs from SEQ ID NO:8 by having a glutamine at position 1077, and lacking a lysine, proline and glutamine at positions 1505-1507 (*see*, p. 37, lines 19-29 of WO 96/28537).

WO 96/28537, Chen *et al.* and Deschênes *et al.* were cited as affecting the inventive step of the claims. Chen *et al.* and Deschênes *et al.* were cited to show that SCN5A mutants were known prior to Applicant's filing date. These documents, however, do not bridge the gap between WO 96/28537 and this application, as the disclosed sequences differ from SEQ ID NO:8. Deschênes *et al.* described six SCN5A mutations (*i.e.*, ΔKPQ, N1325S, R16441I, E1784K, R1512W and R1432G); and Chen *et al.* described four SCN5A mutations (*i.e.*, R1232W, T1620M, +AA and ΔA).

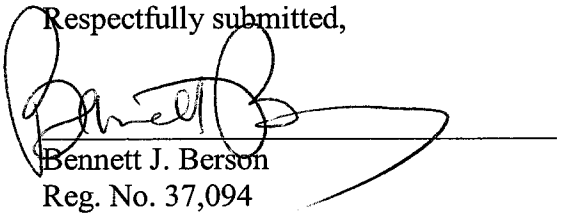
Applicants also cancel Claims 17 and 18.

In view of Applicants' comments above, no cited document adversely affects the novelty or non-obviousness of the claims as amended.

Fees

A petition for a one-month extension of time accompanies this response so that it will be deemed to have been timely filed. No other extension of time is believed due; however, if any additional extension is due, in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to Deposit Account No. 17-0055. Likewise, no additional fees are believed due; however, if any fees are due, in this or any subsequent response, please charge Deposit Account 17-0055.

Respectfully submitted,



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